REMARKS

Claims 1-11 are pending.

I. The rejection of claims 1-9 and 11 under 35 U.S.C. § 103(a) as obvious over Geusens et al., J of Clin Densitometry, 2001;4:389-394

Claims 1-9 and 11 have been rejected as obvious over Geusens et al., J of Clin Densitometry, 2001;4:389-394 ("Geusens"). According to the Examiner, Geusens discloses the case history of an 18-year old boy treated with intravenous pamidronate (a bisphosphonate) for extreme back pain resulting from multiple vertebral fractures. The pamidronate was administered intermittently over a nine month period. The patient's back pain progressively improved. *See,* Office Action, page 3.

The Examiner acknowledges that Geusens does not teach treating chronic spinal mechanical pain, i.e., any back pain lasting more than twelve weeks which is not caused by cancer or an osteoporotic compression fracture. However, the Examiner contends that it would have been obvious to use pamidronate for the treatment of any back pain because Geusens discloses the effectiveness of pamidronate in pain management. *Id.* at 3-4. Applicant respectfully traverses this rejection.

Geusens discloses the well-known use of pamidronate to increase bone density. Every mention of pamidronate (or bisphosphonates generally) in Geusens is quoted below:

- "Bone density was extremely low .... The patient was treated with calcium and vitamin D, calcitonin, biophosphonates, physiotherapy, and progressive mobilization. Glucocorticoids were decreased and could be stopped as the neurologic deficits fully recovered. After 1 yr of treatment with intermittent iv pamidronate, bone density had increased by 40% in the spine and by 25% in the femoral neck despite growth arrest." Geusens, abstract.
- "Since the patient was lying down most of the day, bisphosphonates could not be given orally in view of possible irritation of the esophagus. Therefore,

intermittent iv infusions of pamidronate were given at a dose of 30 mg infusion, 300 mg in total over 9 mo." Geusens, p. 390.

- "Bone density increased by 36% in the spine and by 14% in the femoral neck after 6 mo of treatment with pamidronate and by 40% in the spine and by 25% in the femoral neck after 1 yr of treatment with pamidronate." *Id.*
- "Parenteral pamidronate increased bone density within 6 mo with a further increase in 1 yr. The increase in bone density was much higher than in adults treated with bisphosphonates." *Id.* at 393.
- "How long should biphonsponates be given? We plan to stop bisphosphonate treatment when no further increase in bone density can be detected during follow-up every 6 mo." *Id.*

Thus, bisphosphonates, including pamidronate, are only mentioned in Geusens in relation to bone density. The patient in Geusens did have an improvement in his pain, but other treatments he received, alone or in combination, can account for this improvement. In addition to bisphosphonates, the patient in Geusens received calcium, vitamin D, calcitonin, physiotherapy, progressive mobilization, glucocorticoids, analgesics, and nonsteroidal anti-inflammatory drugs. Geusens, abstract, p 390.

The instant obviousness rejection should be withdrawn because every mention of bisphosphonates in Geusens is made in relation to bone density, not pain. It would only have been obvious to link bisphosphonate administration to pain relief by using the instant specification as a roadmap. This constitutes impermissible hindsight because the rejection was made in reliance upon teachings not drawn from any prior art disclosure, but from the applicant's own disclosure. *See,* MPEP 2145; *In re McLaughlin* 443 F.2d 1392, 1395, 170 USPQ 209, 212 (CCPA 1971) (An obviousness rejection should "not include knowledge gleaned only from applicant's disclosure, such a reconstruction is proper."). *See, In re Deminski*, 796 F.2d 436, 443, 230 USPQ 313, 316 (Fed.Cir.1986); *W.L. Gore & Assocs., Inc. v. Garlock, Inc.,* 721 F.2d 1540, 1553, 220 USPQ 303, 313 (Fed.Cir.1983) *cert. denied*, 469 U.S. 851 (1984). One of ordinary skill in the art, without the benefit of the instant specification, would have understood Geusens to teach that bisphosphonates

increase bone density because this is all that is stated in Geusens, e.g., according to Geusens, the plan is to administer pamidronate to the patient until no there are no further increases in bone density. Geusens does not disclose or suggest any effect of pamidronate on pain.

Accordingly, for the reasons stated above, this rejection should be withdrawn.

II. The rejection of claims 1-9 and 11 under 35 U.S.C. § 103(a) as obvious over Urban et al., Society for Neuroscience Abstracts, 2001;27(1):1326 in view of U.S. Patent No. 6,676,970

The Examiner has rejected claims 1-8, 10 and 11 as obvious over Urban et al., Society for Neuroscience Abstracts, 2001;27(1):1326 ("Urban") in view of U.S. Patent No. 6,676,970 ("Bader"). According to the Examiner, Urban discloses that zoledronate (a bisphosphonate) produces an anti-allodynic effect in rats, and Bader discloses parental zoledronate preparations. The Examiner contends that one of ordinary skill in the art would have been motivated to use intravenous zoledronate to treat pain as an alternative to the subcutaneous formulation disclosed in Urban. *See,* Office Action, pages 4-5. Applicant respectfully traverses this rejection.

Urban discloses that intra-tibial injections of breast tumor cells produced "severe damage to the bone." Urban, abstract. Zoledronate administration resulted in the death of tumor cells. *Id.* The anti-tumor effect of bisphosphonates was known in the art: "Bisphosphonates ... exert cytostatic and pro-apoptotic effects on breast cancer and prostate cancer cells lines similar to those observed with myeloma cell lines." Green JR, Cancer Supplement, 2003;97(3):840-847 (citing publications dated between 1997-2001) (copy attached). The anti-allodynic effect of bisphosphonates in this model occurred as a consequence of treating the cancer. Logically, an agent that kills cancer cells would be expected to improve cancer-related pain as the pressure exerted by the tumor and its in-growth into normal tissues is relieved by tumor shrinkage. Conversely, agents that were well-known analgesics (unlike bisphosphonates), but do not kill cancer cells, had no effect on the cancer-induced allodynia. *See*, Urban (COX-2 inhibitors have "no influence"). No combination of the references suggests that a bisphosphonate would relieve pain independent of its anti-neoplastic effect. No combination of the references suggests that a known cancer-killing agent, i.e., a bisphosphonate, would have an antinociceptive effect in a subject with pain unrelated to

cancer. Accordingly, the instant claims are non-obvious because "chronic spinal mechanical pain" excludes back pain caused by cancer. *See*, specification, page 7, lines 15-16.

For the reasons stated above, this rejection should be withdrawn.

Conclusion

In view of the above remarks, it is respectfully requested that the pending claims be allowed and the case passed to issue.

If there are any other issues remaining, which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Dated: November 19, 2008

Respectfully submitted,

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